ACTA CHEMICA SCANDINAVICA 23 (1969) 3385–3392

N-Isothiocyanatoamines

XII. Preparation and Isomerism of *N,N*-Diisopropyldithiocarbazic Esters

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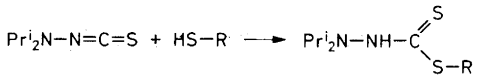
N-Isothiocyanatodiisopropylamine reacts with aliphatic and aromatic thiols to give *N,N*-diisopropyldithiocarbazic esters. The infrared spectra of the latter compounds have been determined in the solid state and in solution and show that *tert*-butyl *N,N*-diisopropyldithiocarbazate is anomalous in that it exists principally in a dipolar form in both states. The ^{1}H NMR spectra have been analyzed by means of a method described previously indicating that solutions of most of the other dithiocarbazic esters also contain mixtures of dipolar and nonpolar forms, though generally with only small amounts of the dipolar isomers. The *cis-trans* isomerism and the magnetic nonequivalence in the methyl signals of the diisopropylamino groups are briefly discussed.

During a study of the reactions between *N*-isothiocyanatodiisopropylamine (I) and amines [1] it was observed that (I) attacked the thiol group in preference to the amino group in the case of aromatic compounds carrying both types of groups. It was also found that in contrast to phenyl isothiocyanate, which reacted with 2-aminoethanethiol with initial formation of the *N*-substituted product,[2] both aliphatic isothiocyanates and the isothiocyanatoamine (I) reacted to give only the *N,S*-disubstituted product. These observations suggested that the reactivity of (I) towards the thiol group is sufficient for dithiocarbazic esters to be prepared by the reaction



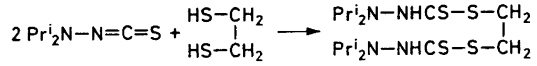
I II–VIII, X–XIII

Table 1. *N,N,*-Diisopropyldithiocarbazic esters $Pr^i_2NNHCSSR$ formed by the reaction of *N*-isothiocyanatodiisopropylamine (I) with compounds containing the thiol group.

Reagent	Prepared	Method	Yield %	M.p. °C	Formula	Analyses (C, H, N, S)
Methanethiol	Methyl *N,N*-diisopropyldithiocarbazate (II)	A	51	64—65	$C_8H_{18}N_2S_2$	Found: 46.75; 8.72; 13.43; — Calc.: 46.56; 8.79; 13.58; —
Ethanethiol	Ethyl *N,N*-diisopropyldithiocarbazate (III)	B	65	37—38	$C_9H_{20}N_2S_2$	Found: 49.28; 9.22; 12.36; 28.95 Calc.: 49.04; 9.15; 12.71; 29.09
1-Propanethiol	Propyl *N,N*-diisopropyldithiocarbazate (IV)	B	64	73.5—74	$C_{10}H_{22}N_2S_2$	Found: 51.40; 9.54; 11.73; 27.07 Calc.: 51.25; 9.47; 11.96; 27.36
2-Propanethiol	Isopropyl *N,N*-diisopropyldithiocarbazate (V)	B	59	64.5—65	$C_{10}H_{22}N_2S_2$	Found: 51.36; 9.52; 11.85; 27.29 Calc.: 51.25; 9.47; 11.96; 27.36
1-Butanethiol	Butyl *N,N*-diisopropyldithiocarbazate (VI)	B	69	45—45.5	$C_{11}H_{24}N_2S_2$	Found: 53.42; 9.78; 10.98; — Calc:. 53.18; 9.74; 11.28; —
2-Methyl-1-propanethiol	Isobutyl *N,N*-diisopropyldithiocarbazate (VII)	B	47	41.5—42	$C_{11}H_{24}N_2S_2$	Found: 53.40; 9.82; 11.07; — Calc.: 53.18; 9.74; 11.28; —
2-Methyl-2-propanethiol	*tert*-Butyl *N,N*-diisopropyldithiocarbazate (VIII)	B	25	92—93	$C_{11}H_{24}N_2S_2$	Found: 53.15; 9.76; 10.93; 25.92 Calc.: 53.18; 9.74; 11.28; 25.81
1,2-Ethanedithiol	1,2-Ethylenebis(*N,N*-diisopropylcarbazate) (IX)	E	49	189—190	$C_{16}H_{34}N_4S_4$	Found: 47.10; 8.14; 13.20; — Calc.: 46.79; 8.34; 13.64; —
Methyl mercaptoacetate	Methoxycarbonylmethyl *N,N*-diisopropyldithiocarbazate (X)	D	76	82—83	$C_{10}H_{20}N_2O_2S_2$	Found: 45.57; 7.59; 10.42; — Calc.: 45.42; 7.62; 10.60; —
Benzenethiol	Phenyl *N,N*-diisopropyldithiocarbazate (XI)	C	30	114—116	$C_{13}H_{20}N_2S_2$	Found: 58.25; 7.39; 10.52; — Calc.: 58.16; 7.51; 10.44; —
2-Mercaptobenzoic acid	2-Carboxyphenyl *N,N*-diisopropyldithiocarbazate (XII)	B	65	145—146	$C_{14}H_{20}N_2O_2S_2$	Found: 54.00; 6.29; 8.87; — Calc.: 53.82; 6.45; 8.97; —
Phenylmethanethiol	Benzyl *N,N*-diisopropyldithiocarbazate (XIII)	D	62	99—100	$C_{14}H_{22}N_2S_2$	Found: 59.70; 7.83; 9.80; — Calc.: 59.53; 7.85; 9.92; —

Few examples exist of the related method of preparation of dithiocarbamic esters from isothiocyanates and thiols. However, to the extent it has been investigated, it has recently been concluded [3] that addition or use of a basic catalyst is essential to secure a good yield. When (I) was allowed to react with different aliphatic and aromatic thiols it was found that addition of bases was unnecessary. This result is in harmony with previous investigations of the reactivity of *N*-isothiocyanatoamines towards amines,[1] hydrazines,[4] phenols,[5] and thioamides,[6] which have given concordant evidence that the reactivity of (I) exceeds that of aliphatic and aromatic isothiocyanates. In the present case, of course, the inherent basicity of (I) may be a contributory cause of the enhanced reactivity. However, all attempts to titrate (I) directly with hydrochloric acid, have failed.

The product data for the reaction between (I) and twelve different thiols are summarised in Table 1. It is seen that the yields of dithiocarbazic esters generally range from 50 to 75 %. However, the yields of the reactions with *tert*-butyl mercaptan and thiophenol were small (25—30 %) for unknown reasons. In the former case, steric hindrance, the dipolar structure of the product (see later), and difficulties in the purification are only three of the possible reasons for the failure to obtain a good yield. All reactions proceeded according to the general scheme given above to give colourless dithiocarbazic esters. If two functional groups are present in the reactant, as in the case of the reaction between (I) and 1,2-ethanedithiol, only the disubstituted product (IX) was obtained.



IX

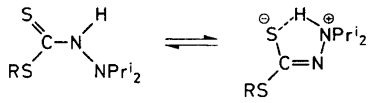
The identity of the products were checked by elemental analysis and by recording their infrared spectra in potassium bromide pellets. With the exception of the compounds VIII and XII all infrared spectra displayed two absorptions indicative of the nonpolar thioester structure. The first band was situated between 3140 and 3150 cm^{-1}, well resolved from other absorption, and of medium strength. This band can without doubt be assigned to NH stretching vibrations. It is found at rather low wavenumbers owing to the resonance stabilization of the dithiocarbazates by structures with positively charged nitrogen and negatively charged sulfur. The second absorption was easily recognized as a strong and somewhat broad band with maximum in the region between 1500 and 1510 cm^{-1}. A systematic deuterium labelling study of the infrared spectra of dithiocarbazic acids [7] has shown this band to originate principally from a stretching motion of the thioureide NCS skeleton thus parallelling the "B band" of thioureides.[8]

Two compounds, VIII and XII, do not exhibit these characteristics in their infrared spectra. The only structural entity these exceptions have in common is a sterically very bulky group attached to the sulfur atom of the *N*,*N*-diisopropyldithiocarbazate part of the molecule. Both compounds showed

a complete lack of absorption corresponding to the two bands discussed above. Instead a new typical absorption pattern appeared in the region between 2500 and 3100 cm^{-1} consisting of a very broad absorption with several submaxima, and assigned to the stretching vibration of the hydrogen part of a substituted ammonium group. Since XII contains a free carboxyl group other arguments can be advanced to explain the absorption pattern of XII, but the *tert*-butyl ester (VIII) must definitely have a structure different from that of the other alkyl esters. Experience of dipolar thiocarbazoyl compounds [9] has led us to believe that the pattern observed arose from a dipolar form of VIII (form C, Table 2). Since the infrared spectrum of VIII in various solutions was found to have characteristics similar to the KBr-spectrum, the spectra of II—XIII were also recorded in solution. In almost all cases small amounts of absorption could be detected in the region between 2500 and 3000 cm^{-1} different from the usual sharp bands of alkyl groups *etc.*, *i.e.* it was probable that these compounds also contained small amounts of a dipolar form in solution. The structure of the species in equilibrium were therefore investigated by ^1H NMR spectroscopy on II—XIII in different solvents.

Previously [10] it was described how the ^1H NMR spectra of mixtures of nonpolar and dipolar forms of acyl- and thiocyl *N,N*-diisopropylhydrazines provide information about the structure and relative amount of the individual forms.

Table 2. Magnetic nonequivalence (Δ, Hz) of the methyl groups of the diisopropylamino group of the two forms A and C present in 5 % solutions of *N,N*-diisopropyldithiocarbazic esters at 40°C:



A C

R	Solvent	Form A		Form C	
		%	Δ	%	Δ
CH_3 (II)	CCl_4	96	3.7	4	0
	$(CD_3)_2SO$	90	3.4	10	0
	$CDCl_3$	80	4.9	20	0
CH_3CH_2 (III)	CCl_4	98	3.6	2	not obs.
	$CDCl_3$	89	5.0	11	not obs.
$CH_3CH_2CH_2$ (IV)	CCl_4	100	3.8	0	—
	$CDCl_3$	85	4.8	15	1.0
$(CH_3)_2CH$ (V)	CCl_4	99	3.3	1	0
	$CDCl_3$	90	4.6	10	0
$CH_3CH_2CH_2CH_2$ (VI)	$CDCl_3$	85	4.9	15	0
$(CH_3)_2CHCH_2$ (VII)	$CDCl_3$	91	not obs.	9	1.0
$(CH_3)_3C$ (VIII)	$CDCl_3$	*ca.* 10	3.0	*ca.* 90	0
CH_3OOCCH_2 (X)	$CDCl_3$	*ca.* 50	5.9	*ca.* 50	1.9
C_6H_5 (XI)	$CDCl_3$	*ca.* 60	5.8	*ca.* 40	not obs.
$C_6H_5CH_2$ (XIII)	$CDCl_3$	65	3.9	35	3.1

It was shown that the dipolar species could be unambiguously identified by virtue of the coupling between the NH proton and the methine protons of the diisopropylamino group. The nonpolar species differed in the relative positions of the diisopropylamino group and the sulfur atom of the thiocarbonyl group. If they were in a *trans* position to each other the signal from the methyl protons of the diisopropylamino group was a doubled doublet, *i.e.* the protons were nonequivalent, but in the cases where the groups were in mutually *cis* positions nonequivalence was not observed except on cooling to temperatures in the neighbourhood of −40°C.

By applying these criteria (and occasionally others mentioned in the paper) the ^{1}H NMR spectra were concluded to result from mixtures of a nonpolar form A and a dipolar form C, the structures of which are shown in the upper part of Table 2. The table shows that the A form predominates in the ^{1}H NMR spectra of the simple alkyl esters II—VII, but the C form predominates in the *tert*-butyl ester VIII. This result provides further confirmation of the conclusion [10] that the introduction of a sterically bulky group is a contributing reason for the diisopropylamino group to achieve a *trans* position relative to the former group. Other effects are also operative as shown by the data for the esters X—XII. In these cases electronegative groups are attached to the sulfur atom resulting in a stabilization of the dipolar form C relative to the A form.

The observation of magnetic nonequivalence (Table 2) of the methyl groups of the diisopropylamino group, inferred from the splitting of the doublets by 3—6 Hz, is in accordance with our observations on related systems [10] that even small (*e.g.* methyl) substituents *cis* to the diisopropylamino group are sufficient to hinder inversion of the nitrogen atom carrying the isopropyl groups. The absence of nonequivalence in many of the C forms of dithiocarbazic esters at 40°C indicates [9,10] the mean lifetime of the mobile hydrogen atom on the positively charged nitrogen to be small, *i.e.* the inversion of the diisopropylamino group is rapid measured by the ^{1}H NMR time scale. It has previously been showed that when electropositive substituents are attached to the thiocarbonyl group (*e.g.* thioacyl *N*,*N*-diisopropylhydrazines [10]) the temperature limit for detection of nonequivalence is as low as 20—30°C, but that electronegative substituents raise this limit to above 50°C (*e.g.* thiocarbamoyl and thiocarbazoyl *N*,*N*-diisopropylhydrazines [10]). Since the nonequivalence of thioformyl *N*,*N*-diisopropylhydrazine was shown to be a borderline case with disappearance of nonequivalence at *ca.* 40°C the present results with dithiocarbazic esters indicate the electronegative and the electropositive effects of the SR group almost to outbalance each other.

Since the simple spectrum of methyl *N*,*N*-diisopropyldithiocarbazate (II) permits an unambiguous assignment of peaks it was chosen for investigation of the temperature dependence of the nonequivalence of a nonpolar diisopropylamino group. The values of the chemical shifts (Table 3), with exception of the two methyl doublets of the diisopropylamino group change continuously with rising temperature. The most reasonable explanation for the unchanged position of these doublets is that the methyl groups are locked in a fixed conformation limited by an almost symmetrical potential barrier. It is also perhaps possible that they rotate, more or less freely, between several rotamers in which they experience identical fields. At *ca.* 50°C the doublet at lowest field

Table 3. Temperature dependence (20 % solution in $CDBr_3$) of the ^1H NMR chemical shifts[a] (τ, ppm), the coupling constants (J, Hz) and the magnetic non-equivalence (Δ, Hz) of the methyl groups of the isopropyl groups in the non-polar form of methyl *N*,*N*-diisopropyldithiocarbazate (II).

Temperature °C	CH_3			CH	NH
	Chem. shift	J	Δ	Chem. shift	Chem. shift
10	8.873	6.6	4.2	6.71	1.37
	8.803	6.6			
40°	8.873	6.6	3.9	6.73	1.62
	8.808	6.6			
50°	8.870	6.6	3.5	6.73	1.70
	8.812	6.6			
60°	8.863	6.6	2.0	6.73	1.76
	8.830	6.6			
65°	8.858	6.6	0	6.76	1.81
80°	8.842	6.6	0	6.75	1.87
100°	8.838	6.6	0	6.75	1.97

[a] The values given in the table are the centers of the multiplets.

Table 4. Temperature dependence (20 % solution in $CDCl_3$) of the ^1H NMR chemical shifts[a] (τ, ppm), the coupling constants (J, Hz), and the magnetic non-equivalence (Δ, Hz) of the methyl groups of the isopropyl groups in the dipolar form of *tert*-butyl *N*,*N*-diisopropyldithiocarbazate (VIII).

Temp. °C	CH_3			CH		NH	
	Chem. shift	J	Δ	Chem. shift	J	Chem. shift	J
−40	8.522	6.6	2.7	*ca.* 6.12	—	−0.75	5.0
	8.477	6.6		*ca.* 6.02			
−30	8.528	6.8	2.7	*ca.* 6.13	—	−0.78	5.0
	8.483	6.8		*ca.* 6.04			
−20	8.536	6.7	2.6	*ca.* 6.15	—	−0.82	4.9
	8.492	6.7		*ca.* 6.05			
−10	8.540	6.7	2.7	6.18	*ca.* 5.3	−0.83	5.0
	8.495	6.8		6.09			
0	8.547	6.8	2.6	6.17	5.1	−0.85	—
	8.503	6.8		6.08			
+10	8.547	6.7	2.4	6.18	5.0	−0.88	—
	8.507	6.8		6.10			
+20	8.552	6.7	2.1	6.20	5.1	−0.92	—
	8.517	6.8		6.11			
+25	8.551	6.7	1.8	6.20	5.1	−0.95	—
	8.521	6.9		6.11			
+30	*ca.* 8.534	*ca.* 6.8	*ca.* 0.5	6.20	5.1	−0.95	—
				6.12			
+40	8.538	6.8	0	6.21	5.0	−0.97	—
				6.13			
+60	8.541	6.8	0	6.23	4.9	−1.00	—

[a] The values given in the table are the centers of the multiplets.

starts to move towards the other methyl doublet, the position of which is much less changed. Above 65°C only one doublet results and it changes continuously with rising temperature. This latter variation is attributed to a temperature dependent population of the rotamers involved. In summary, none of these observations establish that the magnetic nonequivalence arises from hindered inversion of the nitrogen atom of the diisopropylamino group, but neither, on the other hand, do they contradict this hypothesis.

Table 4 summarizes the most important ^{1}H NMR results for the dipolar form of the *tert*-butyl ester (VIII). Proof of the presence of the dipolar structure C was obtained from observation of the coupling between the NH proton with the neighbouring methine protons of the diisopropylammonio group. From −40°C to +60°C this produced a doubling of the septuplet from the methine protons with a spacing of *ca.* 5 Hz and below −10°C the NH signal sharpened sufficient to observe the identical spacing of this triplet. The coupling was finally ascertained by shaking with deuterium oxide which caused the two septuplets to collapse to one septuplet. Since the nonequivalence of the methyl signals of the isopropyl groups disappeared just above 30°C, where the CH—NH coupling was unchanged, the reasons previously given for the nonequivalence in 1-(*N*,*N*-diisopropylthiocarbazoyl)imidazole [9] apply also in this case and will not be repeated. The only difference between the two cases is their behaviour in the temperature range below the limit for nonequivalence. As a result of an (accidental) simultaneous change of both signals towards higher field on heating, VIII had an almost unchanged spacing between the methyl doublets, whereas the nonequivalence decreased in the case of the imidazole derivative.

EXPERIMENTAL

Conditions and equipment used for the physical measurements were those described in part II of this series.[11]

Reaction of (I) with the thiols listed in Table 1. The directions given below refer to entry ("Method"), Table 1. *Method A.* A slow stream of methanethiol was introduced, over a period of 10 min into a solution of (I) in ethanol (*ca.* 10 %).[1] After evaporation of the solvent and unreacted methanethiol the residue was recrystallized from pentane. *Method B.* The thiol was added in small portions to an ethanolic solution of (I) (10 %) and in most instances an exothermic reaction was observed. The reaction mixture was allowed to stand for 24 h and water was added dropwise to induce precipitation. By cooling and scratching crystallization was effected and the product was finally recrystallized from ethanol, eventually from a water-ethanol mixture. *Method C.* As method B, but recrystallization was replaced by extraction of the crude product with pentane. Evaporation of the pentane furnished the analytically pure product. *Method D.* The thiol was added in small portions, with shaking or stirring, to a 10 % solution of (I) in pentane. The crystalline product was filtered off and recrystallized from pentane or a mixture of pentane and benzene. *Method E.* The thiol was added to an ethanolic solution of (I). After a few minutes the product was filtered off and washed thoroughly with boiling ethanol.

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Received May 9, 1969.